

## INTRODUCTION

The probability that a resident of the United States will develop cancer at some point in his or her lifetime is 1 in 2 for men and 1 in 3 for women (ACS 1999). Nearly everyone's life has been directly or indirectly affected by cancer. Most scientists involved in cancer research believe that many cancer cases may be associated with the environment in which we live and work. In this context, the environment is anything that people interact with including lifestyle choices, such as what we eat, drink, or smoke; natural and medical radiation, including exposure to sunlight; workplace exposures; drugs; socioeconomic factors that affect exposures and susceptibility; and substances in air, water, and soil (OTA 1981). Other factors that play a major role in cancer development are infectious diseases, aging, and individual susceptibility, such as genetic predisposition. We rarely know what environmental factors and conditions are responsible for the onset and development of cancers; however, in some cases, we have some understanding of cancer development, especially for cancers related to certain occupational exposures or the use of specific drugs. Many experts firmly believe that much of the cancer associated with the environment may be avoided (Tomatis *et al.* 1997).

The people of the United States, concerned about the relationship between their environment and cancer, have asked, through the U.S. Congress, for information about substances that are known or appear likely to cause cancer (i.e., to be carcinogenic). Section 301(b)(4) of the Public Health Service Act, as amended, provides that the Secretary of the Department of Health and Human Services (DHHS) shall publish a biennial report that contains the following information:

- A) A list of all substances (1) which either are known to be human carcinogens or may reasonably be anticipated to be human carcinogens and (2) to which a significant number of persons residing in the United States are exposed.
- B) Information concerning the nature of such exposure and the estimated number of persons exposed to such substances.
- C) A statement identifying (1) each substance contained in this list for which no effluent, ambient, or exposure standard has been established by a Federal agency and (2) for each effluent, ambient, or exposure standard established by a Federal agency with respect to a substance contained in this list, the extent to which such standard decreases the risk to public health from exposure to the substance.
- D) A description of (1) each request received during the year to conduct research into, or testing for, the carcinogenicity of a substance and (2) how the Secretary and other responsible entities responded to each request.

The Report on Carcinogens (RoC) is an informational scientific and public health document that identifies and discusses substances (including agents, mixtures, or exposure circumstances) that may pose a carcinogenic hazard to human health. It serves as a meaningful and useful compilation of data on (1) the carcinogenicity (whether it causes cancer), genotoxicity (whether it causes damage to genes), and biologic mechanisms (how it works in the body) of the

listed substances in people and/or in animals, (2) the potential for human exposure to these substances, and (3) Federal regulations to limit exposures. The RoC does not present quantitative assessments of the carcinogenic risk of these substances. Listing of substances in the RoC, therefore, does not establish that these substances present carcinogenic risks to individuals in their daily lives. Such formal risk assessments are the responsibility of the appropriate federal, state, and local health regulatory and research agencies.

The substances listed in the RoC are either known or are reasonably anticipated to cause cancer in humans under certain exposure circumstances. In many cases, cancers resulting from exposures to the listed substances may require exposures for prolonged periods of time. For example, smoking tobacco is known to cause cancer in humans; however, not all people who smoke develop smoking-related cancers. Some substances or circumstances, however, need only short exposures to cause cancer. Examples include certain occupational exposures to asbestos or bis(chloromethyl) ether. The carcinogenic hazard that listed substances pose to any one person depends on many factors. Among these are the amount and duration of exposure to the substance, an individual's susceptibility to the carcinogenic action of the substance, and the intrinsic carcinogenicity of the substance. Because of these considerations, the RoC does not attempt to rank substances according to the relative carcinogenic hazards.

### **Potential Beneficial Effects of Listed Carcinogens**

As stated above, the RoC is a cancer health hazard identification document; therefore, it is not within the scope of this report to address potential *benefits* of exposures to certain carcinogenic substances in special situations. For example, numerous drugs used in typical cancer treatment or other medical treatment programs have been shown to increase the frequency of primary or secondary cancers in patients undergoing treatment for specific diseases. In these cases, the benefits of using the drug for treating or preventing a specific disease outweigh the added cancer risks associated with its use. Personal decisions concerning voluntary exposures to carcinogenic substances should be based on information that is beyond the scope of the RoC. Individuals should *not* make decisions concerning the use of a given drug, or any other listed substance, based solely on the information contained in the RoC. Decisions of this type should be made only after consulting with a physician or other appropriate specialist.

### **Identification of Carcinogens**

For many years, government research agencies (including the National Toxicology Program), industries, academia, and other research organizations have studied various substances to identify those that may cause cancer. Much of this information on specific chemicals or occupational exposures has been published in the scientific literature or in publicly available and peer-reviewed technical reports; this literature is a primary source of information for identifying and evaluating substances for listing in the RoC. Many of the listed substances also have been reviewed and evaluated by other organizations, including the International Agency for Research on Cancer (IARC) in Lyon, France, the Environmental Protection Agency of the State of California, and other U.S. Federal and international agencies.

Both human and animal studies are used to evaluate whether substances are possible human carcinogens. The strongest evidence for establishing a relationship between exposure to any given substance and cancer in humans comes from epidemiological studies—the study of the occurrence of a disease in a defined population and the factors that affect its occurrence.

These studies of human exposure and cancer are difficult. They must rely on natural, not experimental, exposures in humans, and therefore, must consider many factors that may affect cancer prevalence besides the chemical or exposure under study, as well as the latency period for cancer development. The exposure to the carcinogen often occurs many years (sometimes 20 to 30 years or more) before the first sign of cancer appears. Another valuable method for identifying substances as potential human carcinogens is the long-term animal bioassay. These bioassays provide accurate information about dose and duration of exposure and are less affected than epidemiology studies by possible interactions of the substance with other chemicals or modifiers. In these studies, the substance is given to one or, usually, two laboratory rodent species over a range of doses for nearly the entire life of the animals, with all experimental conditions carefully chosen to maximize the likelihood of identifying any carcinogenic effects (Huff 1999).

It is not possible to predict with complete certainty, from animal studies alone, which substances will be carcinogenic in humans; however, generally known human carcinogens that have been tested adequately in laboratory animals also produce cancers in laboratory animals. In many cases, a substance was first found to cause cancer in animals and only later was confirmed to cause cancer in humans (Huff 1993). Experimental cancer research is based on the scientific assumption that substances causing cancer in animals will have similar effects in humans. How laboratory animals respond to substances (including cancer and other illnesses) does not always strictly correspond to how people will respond; however, laboratory animal studies remain the best tool for detecting potential human health hazards of all kinds, including cancer (OTA 1981, Tomatis *et al.* 1997).

### **Listing Criteria**

The criteria for listing an agent substance, mixture, or exposure circumstance in the RoC are as follows:

***Known To Be Human Carcinogen:***

**There is sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.**

***Reasonably Anticipated To Be Human Carcinogen:***

**There is limited evidence of carcinogenicity from studies in humans, which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded,**

**or**

**there is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) in multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset,**

**or**

**there is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous Report on Carcinogens as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.**

**Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to, dose response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive sub-populations, genetic effects, or other data relating to mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals, but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans.**

It should be emphasized that the category "*known to be human carcinogen*" requires evidence from human studies. This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question, which can be useful for evaluating whether a relevant cancer mechanism is operating in people. The listing criteria presented here were first adopted for use in the Eighth RoC, which was published in 1997. Listing criteria for substances listed in earlier editions are outlined in the introductions to those editions.

## Preparation of the RoC

Within the DHHS, the Secretary has delegated the responsibility for preparing the RoC to the National Toxicology Program (NTP). The process used to prepare the RoC involves several levels of review of the nominations considered for listing in or delisting (removal) from the RoC. Opportunities for public comment and participation are an integral part of the review process.

Nominations for listing in or delisting from the RoC are received from a number of sources. Periodic requests for nominations from the public are published in the *Federal Register*, the NTP Liaison Office Update, and other appropriate publications. The NTP actively solicits nominations from member agencies of the NTP Executive Committee.<sup>1</sup> Nominations for the RoC also come from reviews of the literature performed by the NTP. Potential nominations are identified from such sources as the NTP Rodent Bioassay Technical Reports, the IARC Monographs, the State of California Environmental Protection Agency's Carcinogen List, and other similar sources.

Two Federal scientific review groups and one non-governmental scientific peer-review body (a subcommittee of the NTP Board of Scientific Counselors) evaluate the nominations for listing in or delisting from the RoC. Each group reviews the relevant data on the carcinogenicity of the substances nominated and the exposure of U.S. residents to the substances. The members of these three review groups may be found in Appendix D, List of Participants.

A substance nominated for listing or delisting will be evaluated initially by a RoC Review Committee (RG1), composed of scientists from the National Institute of Environmental Health Sciences (NIEHS/NTP). The RG1 will decide whether the information provided is sufficient to merit further consideration. If the RG1 decides that the nomination warrants consideration, the decision will be announced in the *Federal Register*, trade journals, and NTP publications to solicit public comment. The NTP will then begin an independent search of the literature and prepare a background document for the nominated substance. The background document emphasizes information concerning the carcinogenicity and related toxicological evidence for the substance nominated. The document may also include information on exposure provided by study reports and monographs. After reviewing this document, the RG1 makes a formal recommendation to the Director, NTP, for listing or removing the substance in the RoC.

If the RG1 determines that a nomination does not contain sufficient information to warrant consideration by the NTP, the nomination is returned to the original nominator, who is invited to resubmit the nomination with additional justification, such as new experimental data or exposure information. The reason why the nomination will not be reviewed, is also published in the *Federal Register*, trade journals, and NTP publications and is included in subsequent editions of the RoC, with the reason(s) why the nomination was not considered further. The decision is also forwarded to the NTP Board of Scientific Counselors and the NTP Executive Committee.

The second Federal scientific group to review nominations to the RoC is the NTP Executive Committee Interagency Working Group (RG2). The RG2 is a governmental interagency group that provides a second, independent assessment of whether the information

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<sup>1</sup> Agencies represented on the NTP Executive Committee include: Agency for Toxic Substances and Disease Registry (ATSDR), Consumer Product Safety Commission (CPSC), Environmental Protection Agency (EPA), Food and Drug Administration (FDA), National Center for Environmental Health (NCEH/CDC), National Institute for Occupational Safety and Health (NIOSH), Occupational Safety and Health Administration (OSHA), Department of Health and Human Services (DHHS), National Institutes of Health (NIH), National Cancer Institute (NCI), and National Institute of Environmental Health Sciences/NTP (NIEHS/NTP).

available for the nomination warrants its listing in or delisting from the RoC, and makes its recommendations to the Director, NTP.

External peer review of the nominations is performed by a subcommittee of the NTP Board of Scientific Counselors. The subcommittee reviews nominations in open, public meetings. Prior to public review, a notice is published in the *Federal Register*, NTP newsletters and web pages, and other appropriate publications, again soliciting public comment on the nominations. The notice also invites interested groups or individuals to submit written comments or to address the subcommittee during the public review meeting. Upon completion of its review, the subcommittee provides its recommendations to the Director, NTP, for listing in or delisting from the RoC.

Following the Board Subcommittee review, an announcement is published in the *Federal Register*, NTP newsletters and web pages, and other appropriate publications that contains the recommendations of all three scientific review groups and solicits final public comment on the nominations. The recommendations of the three scientific review groups and all public comments are provided to the NTP Executive Committee, which reviews this information and provides the Director, NTP, with its recommendations. All recommendations and public comments are then reviewed by the Director, NTP, who subsequently forwards the RoC containing his or her listing recommendations to the Secretary, DHHS. Upon review and approval by the Secretary, the RoC is then submitted to Congress, and a notice of the RoC publication, indicating all newly listed or removed agents, substances, mixtures, or exposure circumstances is published in the *Federal Register*, NTP newsletters and web pages, and other appropriate publications.

### **Estimation of Exposure**

The RoC is required to list only substances to which a significant number of people living in the United States are exposed. Generally, substances to which very few people are exposed are not listed. Some substances that have been banned or restricted in use (e.g., safrole, arsenical pesticides, and mirex) are listed either because people who were previously exposed remain potentially at risk or because these substances are still present in the environment.

The RoC also is required to provide information about the nature of exposure and the estimated number of people exposed to listed substances. Four of the agencies participating with the NTP in the preparation of the Tenth Edition of the RoC—the Consumer Product Safety Commission (CPSC), U.S. Environmental Protection Agency (EPA), Food and Drug Administration (FDA), and Occupational Safety and Health Administration (OSHA)—are responsible for regulating hazardous substances and limiting the exposure to and use of such substances. Information on use, production, and exposure in each entry of the RoC is reviewed by staff members from these four regulatory agencies. Because there is typically little available information, estimating the number of people who could be exposed, and the route, intensity, and duration of exposure for each substance, is a very difficult task. This RoC attempts to respond to these questions; adequate answers that could be obtained are included in Section III.

The National Institute for Occupational Safety and Health (NIOSH) has conducted two occupational surveys: National Occupational Hazard Survey (NOHS), conducted from 1972 to 1974, and the National Occupational Exposure Survey (NOES), conducted from 1981 to 1983. These surveys have yielded potential exposure data for many listed substances. Although dated,

NOES estimates are provided in the profiles of the substances where available, and NOHS figures are given in some profiles if no other data are available.

### **Regulatory Status**

The RoC is required to identify each listed substance for which no standard on exposure or release into the environment has been established by a Federal agency. The Tenth Edition of the RoC adds to the description of each substance a summary of Federal regulations by the participating agencies.<sup>2</sup> Some of these standards and regulations have been enacted for reasons other than the carcinogenicity of the substance, for instance, to prevent other illness or to improve the quality of food or the environment. Solid or liquid wastes or wastes discharged into the air may contain carcinogens, yet these may be regulated as toxic substances or hazardous pollutants and not specifically as carcinogens. If these regulations reduce exposure to carcinogens, then the cancer risk posed by such substances will likely decrease. The regulations tables and text of the substance profiles in the Ninth RoC have been updated in the Tenth Edition of the RoC.

### **Estimation of Risk Reduction**

For each effluent, ambient, or exposure standard established by a Federal agency for a listed substance, the RoC is required to state the extent to which, on the basis of available medical, scientific, or other data, the implementation of that standard decreases the risk to public health from exposure to the substance. This statement requires quantified information on how much protection from cancer the public receives from established Federal standards.

Estimating the extent of health protection is perhaps the most difficult task in preparing the RoC. One reason for this difficulty is that most Federal laws concerned with reducing cancer risk have been enacted only within the last 20 to 25 years. Typically, a long time passes between the initial exposure to a carcinogen and the onset of disease, and therefore, it is still too early to adequately determine how much the Federal standards and other regulations have decreased the human cancer risk. Also, estimating future risk reduction requires information on past exposure levels for comparison, but such information often is not available or is inaccurate.

The carcinogenic risk (i.e., the probability of developing cancer) depends on many things, including the intensity, route, and duration of exposure to a carcinogen people experience. Different people may respond differently to similar exposures, depending on their age, sex, nutritional status, overall health, genetics, and many other factors. Only in a few instances can risk be estimated with complete confidence, and these estimations require studies of long-term human exposures and cancer incidence in restricted environments, which are rarely available.

One possible way to provide quantitative estimates of risk reduction might be to assume that the cancer risk is directly proportional to exposure. This approach also presumes that data exists on past and present exposure levels, or that all workplace conditions comply with regulations, but only rarely do we have information supporting these assumptions. Despite these

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<sup>2</sup>Throughout these volumes, NIOSH recommendations are included in the tables of regulations. Although NIOSH is not a regulatory agency, the NIOSH findings often are used to formulate regulatory actions.

limitations, it is reasonable and prudent to accept that reducing exposure, for any reason, particularly to substances shown to be carcinogenic in experimental animals, will decrease the incidence of cancer in people (Tomatis *et al.* 1997). This relationship is the basis of current regulatory policies that aim to lower human exposure to cancer-causing substances, and thereby, improve public health.

### **Listing, and Delisting Substances in the Tenth Edition of the RoC**

The Tenth Edition of the RoC contains 228 entries, 15 of which have not appeared in earlier RoCs. The Tenth Edition of the RoC also changes the listing of beryllium and beryllium compounds from *reasonably anticipated to be human carcinogens* to *known to be human carcinogens*, with corresponding revisions of the earlier profile for these chemicals. The Tenth Edition of the RoC lists estrogens, steroidal as *known human carcinogens*. This listing of steroidal estrogens supersedes the previous listing of individual estrogens in the RoC (including conjugated estrogens, estradiol-17 $\beta$ , estrone, ethinylestradiol, and mestranol) and applies to all chemicals of this steroid class. The profile for steroidal estrogens includes information on carcinogenicity, properties, use, production, exposure, and regulations for steroidal estrogens as a class, as well as some specific information for individual estrogens.

Reviews also were conducted for the following substances or exposure circumstances nominated for listing, changing their listing, or delisting from the Tenth Edition of the RoC:

- ◆ Trichloroethylene (TCE) was listed in the Ninth RoC as *reasonably anticipated to be a human carcinogen* based on limited evidence of carcinogenicity from studies in humans and sufficient evidence of malignant tumor formation in experimental animals. TCE was reviewed for a possible change in listing to a *known human carcinogen* in the Tenth Edition of the RoC based on the publication of human studies, after the initial RoC listing, reporting that occupational exposure to TCE resulted in elevated incidence and mortality rates for liver and kidney cancer in workers. An overall analysis of cohort studies, in which exposures were best characterized, found that occupational exposure to TCE was associated with an excess of cancer incidence for liver cancer, kidney cancer, non-Hodgkin s lymphoma, prostate cancer, and multiple myeloma, with the strongest evidence for the first three cancers. Elevated risks for mortality were also observed for Hodgkin s disease, multiple myeloma, cervical cancer, and liver cancer. Nevertheless, these studies are based on a relatively small number of exposed cases and may be confounded by exposure to other solvents and other risk factors. Although exposure was characterized less accurately in case-control studies, elevated risks for kidney cancer, liver cancer, Hodgkin s disease, non-Hodgkin s lymphoma, and cervical cancer were observed, supporting the findings of the cohort studies. Upon completion of the review, it was determined that the listing of TCE should remain as *reasonably anticipated to be a human carcinogen*, based on limited evidence of carcinogenicity from studies in humans and sufficient evidence of malignant tumor formation in experimental animals.
- ◆ Talc, both containing asbestiform fibers and not containing asbestiform fibers, was nominated for possible listing in the Tenth Edition of the RoC. The formal review of the relevant information available concerning exposure and the possible carcinogenic potential of both forms of talc found that there has been considerable confusion over the mineral nature and consequences of exposure to talc, both containing asbestiform

fibers and not containing asbestiform fibers. It is evident that the literature on both forms of talc, with a few exceptions, provides an inadequate characterization of the actual materials under study to enable one to reach definitive conclusions concerning the specific substances responsible for the range of adverse health outcomes reported. Because of this situation, the NTP decided to defer consideration of the listing of talc, both containing and not containing asbestiform fibers, in the RoC. Deferring the consideration of talc does not address the concerns raised during the review process over the excess lung cancers reported in people who were exposed to talc containing asbestiform fibers, or an apparent increase in ovarian cancers in women using cosmetic talc. Therefore, the NTP plans to carefully review the literature on both forms of talc to determine whether a clear definition of the agent or agents involved in human exposures could be developed for a RoC review and whether additional research to investigate potential carcinogenic hazards of both forms of talc would be appropriate.

- ◆ Toluene diisocyanate (TDI) was nominated to be delisted from the RoC by the Diisocyanates Panel of the Chemical Manufacturers Association. The nomination to delist and the data provided in the Diisocyanates Panel's nomination were reviewed by RG1. Based on the review of all information available concerning the carcinogenicity of TDI, it was determined that no new, relevant data were available to support the delisting of TDI from the RoC. TDI remains listed in the Tenth Edition of the RoC as *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in animals and metabolism studies in humans and animals that show TDI is metabolized to the same carcinogenic metabolite, toluene diamine (TDA), after inhalation (human) and oral (rodent) exposures.
- ◆ Tars and mineral oils are currently listed in the RoC as *known human carcinogens*. Ingle and Traul Pharmaceutical Consultants, Inc., submitted comments which pointed out that Section II (names and synonyms of carcinogens) of the Ninth RoC mistakenly includes wood creosote as a synonym for creosotes discussed in the profile for tars and mineral oils. Wood creosotes have not been evaluated by the NTP and are not listed in the RoC. Wood creosotes are not identified in the Table of Contents or stated in the profile for tars and mineral oils to be either a *known or a reasonably anticipated human carcinogen*. The profile for tars and mineral oils in the Ninth RoC states that coal tar and coal tar pitches and untreated and mildly treated mineral oils are *known to be human carcinogens*; thus, these are the only substances identified in this profile that are listed in the RoC. The original Tars and Mineral Oils profile has been divided into two separate profiles in the Tenth Edition of the RoC, Coal Tars and Coal Tar Pitches and Untreated and Mildly Treated Mineral Oils, to emphasize this distinction.

Section II of this report is a tabulation of the names of all the substances (agents, mixtures, or exposure circumstances) listed in the Tenth Edition of the RoC and is divided into two parts. Section II.A identifies 52 substances as *known to be human carcinogens*. Section II.B identifies 176 substances as *reasonably anticipated to be human carcinogens*.

Section III, Carcinogen Profiles, contains a brief description of each substance with a summary of evidence for its carcinogenicity. These profiles are in alphabetical order, and they include specific references to the original papers used to support the listing of the substance.

The substances or exposure circumstances listed in the Tenth Edition of the RoC may constitute only a fraction of actual *known* or *reasonably anticipated human carcinogens*. The RoC lists only those nominated substances or exposure circumstances for which relevant data exist and have been reviewed and found to meet the listing criteria defined above. As additional substances are nominated, they will be considered and reviewed for possible listing in future RoCs.

Certain manufacturing processes, occupations, and exposure circumstances have been considered by the IARC and are classified by that agency as known to be carcinogenic to humans because of associated increased incidences of cancer among workers in these settings. However, certain aspects of occupational exposures may differ in different parts of the world or may have changed over time; therefore, the manufacturing processes and occupations reviewed by IARC may not apply to past or current occupational exposures in the United States. The NTP has not yet reviewed the data supporting the listing of these occupational situations as posing a carcinogenic hazard to people. In the interest of public health and for completeness, these occupational exposures are found in Appendix A of this RoC, with the corresponding IARC references.

### **Other Information Provided in this RoC**

Section IV of this report provides tables listing requests to the DHHS for research, testing, and other information relating to carcinogenicity, either from other Federal agencies or from within the DHHS, and how the DHHS responded to the requests. Section V details the listing and delisting procedures for the RoC. Section VI of this RoC, which is published on compact disk (CD) as a separate Volume (II), contains a cumulative list of Code of Federal Regulations and *Federal Register* citations for each listing in the Tenth Edition of the RoC.

The Tenth Edition of the RoC also includes eight appendices. Appendix A lists manufacturing processes, occupations, and exposure circumstances classified by the IARC as known to be carcinogenic to humans. Appendix B lists agents, substances, mixtures, or exposure circumstances that were delisted from the RoC. Appendix C lists agents, substances, mixtures, or exposure circumstances reviewed but not recommended for listing in the RoC. Appendix D lists participants who collaborated in preparing the Tenth Edition of the RoC. Appendices E, F, and G are, respectively, a glossary of terms, a list of acronyms and abbreviations, and a list of units of measurement used frequently in the Tenth Edition of the RoC. Appendix H lists the Chemical Abstracts Service Registry Numbers (CASRN) of chemical substances listed in this RoC. The CASRN index indicates the page number where a profile of the substance appears in the Tenth Edition of the RoC and the year the substance was first listed in the RoC.

For more information on the Tenth Edition of the RoC, including how to order a printed copy or access it on the Web, visit the NTP RoC web site at <http://ntp-server.niehs.nih.gov/NewHomeRoc/AboutRoC.html> or contact Dr. C. W. Jameson, National Toxicology Program, Report on Carcinogens, MD EC-14, P.O. Box 12233, Research Triangle Park, NC 27709, telephone (919) 541-4096, fax (919) 541-0144, e-mail [jameson@niehs.nih.gov](mailto:jameson@niehs.nih.gov).

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